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#### Amendments to the Claims:

Please cancel Claim 95 without prejudice or disclaimer, amend Claims 49, 56, 79-80, 83, 88, 90, 92-93, 96-97 and 122, and add new Claims 149-150 as set forth below.

#### 1-48. (Canceled)

49. (Currently amended) A substrate for a protein kinase, wherein the substrate is selected from the group consisting of:

wherein F is phenylalanine, K is lysine, and R is arginine; and wherein the LINKER

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is selected from the group consisting of N-methyl glycine, L-proline, D-proline,

50-55. (Canceled)

56. (Currently amended) A substrate for a protein kinase, wherein the substrate comprises:

a peptide substrate for the protein kinase, wherein the peptide comprises a serine, a threonine, or a tyrosine on a terminal end of the peptide;

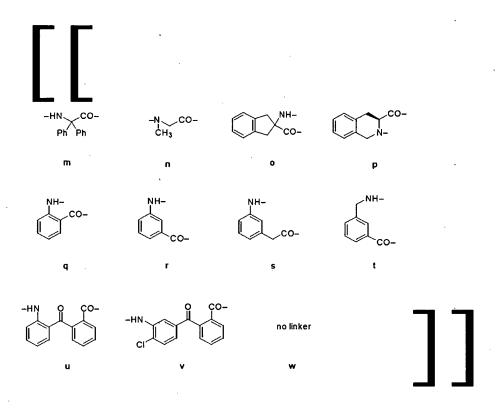
at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide;

wherein the fluorophore is attached directly to the peptide or the a fluorophore is attached to the peptide by a linker selected from the group consisting of

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#### wherein

- (i) the substrate is specific for a protein kinase subtype,
- (ii) the fluorophore is attached to the C-terminal end of the peptide,
- (iii) a fluorophore is attached to each terminal end of the peptide,
- (iv) a first fluorophore is attached to a terminal end of the peptide and a second fluorophore, with photophysical properties distinct from the first fluorophore, is attached to any nonterminal site on the peptide,

; and

- (v) the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative,
- (vi) the fluorophore is attached to the peptide by a linker selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, and a thioether linker, and/or

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(vi)(vii) the substrate further comprises a carbohydrate, a lipid or a nucleic acid.

57. (Previously presented) The substrate of claim 148, wherein the photolabile side chain comprises the structure

- 58. (Original) The substrate of claim 56, wherein the substrate comprises a serine with a photolabile side chain that blocks phosphoryl transfer.
- 59. (Previously presented) The substrate of claim 56, wherein the substrate has the structure

60. (Previously presented) The substrate of claim 148, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% change in fluorescence intensity.

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61. (Previously presented) The substrate of claim 148, wherein after removal of

the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the

terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces

at least a 20% increase in fluorescence intensity.

62. (Previously presented) The substrate of claim 148, wherein after removal of

the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the

terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces

at least a 20% decrease in fluorescence intensity.

63. (Previously presented) The substrate of claim 60, wherein phosphorylation of

the substrate by the protein kinase produces at least a 70% change in fluorescence

intensity.

64. (Original) The substrate of claim 63, wherein phosphorylation of the substrate

by the protein kinase produces at least a 100% change in fluorescence intensity.

65. (Original) The substrate of claim 64, wherein phosphorylation of the substrate

by the protein kinase produces at least a 150% change in fluorescence intensity.

66. (Original) The substrate of claim 65, wherein phosphorylation of the substrate

by the protein kinase produces at least a 250% change in fluorescence intensity.

67. (Previously presented) The substrate of claim 56, wherein the substrate is

specific for a protein kinase subtype.

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68. (Original) The substrate of claim 67, wherein the substrate is specific for

protein kinase C.

69. (Original) The substrate of claim 68, wherein the substrate is specific for

isoforms  $\alpha$ ,  $\beta$ , and  $\gamma$  of protein kinase C.

70. (Withdrawn) The substrate of claim 67, wherein the substrate is specific for

protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca<sup>+</sup>/calmodulin-

dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein

kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase

yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2

kinase.

71. (Previously presented) The substrate of claim 56, wherein the substrate

further comprises a carbohydrate, a lipid or a nucleic acid.

72. (Canceled)

73. (Previously presented) The substrate of claim 56, wherein the fluorophore is

attached to the C-terminal end of the peptide.

74. (Previously presented) The substrate of claim 56, wherein the fluorophore is

attached to the N-terminal end of the peptide.

75. (Previously presented) The substrate of claim 56, wherein a fluorophore is

attached to each terminal end of the peptide.

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76. (Original) The substrate of claim 75, wherein fluorophores with distinct

photophysical properties are attached to different terminal ends of the peptide.

77. (Previously presented) The substrate of claim 56, wherein a first fluorophore is

attached to a terminal end of the peptide and a second fluorophore, with photophysical

properties distinct from the first fluorophore, is attached to any nonterminal site on the

peptide.

78. (Previously presented) The substrate of claim 56, wherein the fluorophore is a

7-nitrobenz-2-oxa-1,3-diazole derivative.

79. (Withdrawn and Currently amended) The substrate of claim 56, wherein the

fluorophore comprises is a fluorescein group derivative.

80. (Withdrawn and Currently amended) The substrate of claim 56, wherein the

fluorophore comprises is selected from the group consisting of a dansyl group derivative,

an acridine group derivative, an Alexa Fluor group derivative, a BODIPY group derivative,

an Oregon Green group derivative, a Rhodamine Green group derivative, a Rhodamine

Red-X group derivative, a Texas Red group derivative, a Cascade Blue group derivative, a

Cascade Yellow group derivative, a Marina Blue group derivative, a Pacific Blue group

derivative, an AMCA-X group derivative, or and a coumarin group derivative.

81. (Canceled)

82. (Withdrawn) The substrate of claim 56, wherein the fluorophore is attached to

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the peptide by a metal chelating linker.

83. (Currently amended) The substrate of claim 56,

A substrate for a protein kinase, wherein the substrate comprises:

a peptide comprising a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide; and

a photolabile side chain attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the substrate, and

wherein the the photolabile side chain comprises the structure

wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

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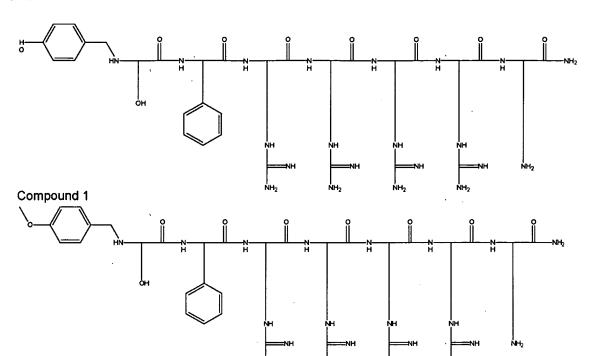
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84. (Withdrawn) The substrate of claim 56, wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of N-methyl glycine, L-proline, D-proline,

#### 85. (Canceled)

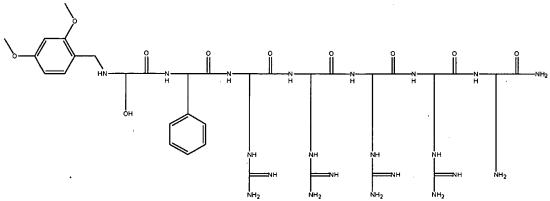
- 86. (Previously presented) A composition comprising the substrate of claim 56, and a carrier.
- 87. (Original) The composition of claim 86, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 88. (Currently amended) A chemical compound selected from the group of compounds consisting of:

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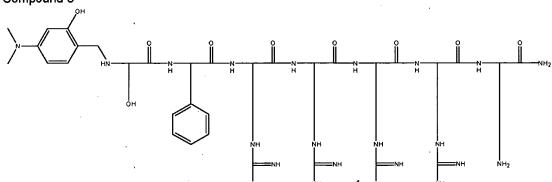
# Compound 2

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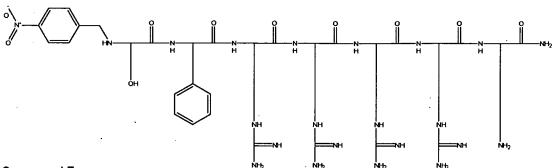
# Compound 4

# Compound 5



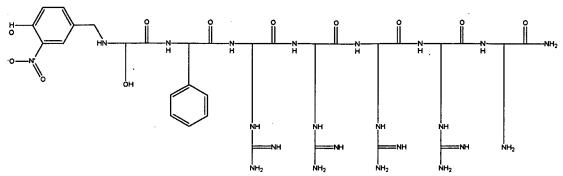
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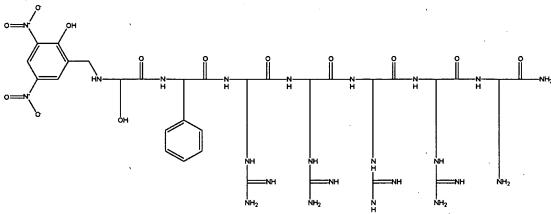


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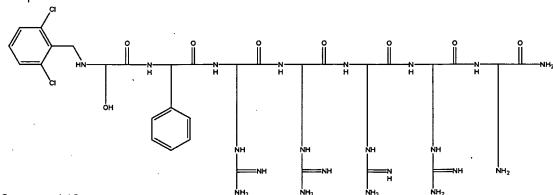
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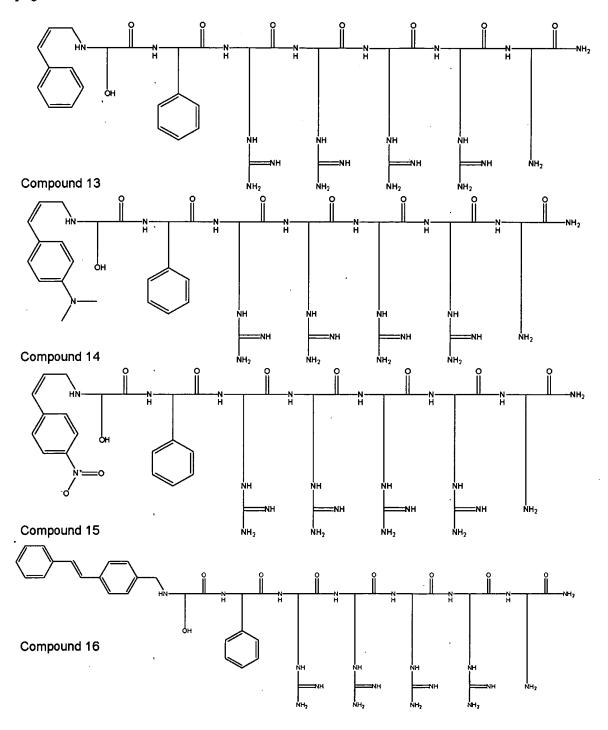
# Compound 10



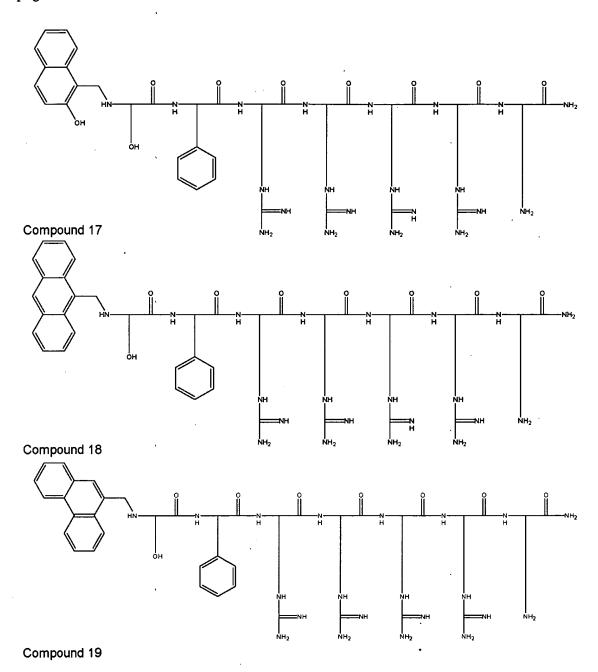
# Compound 11



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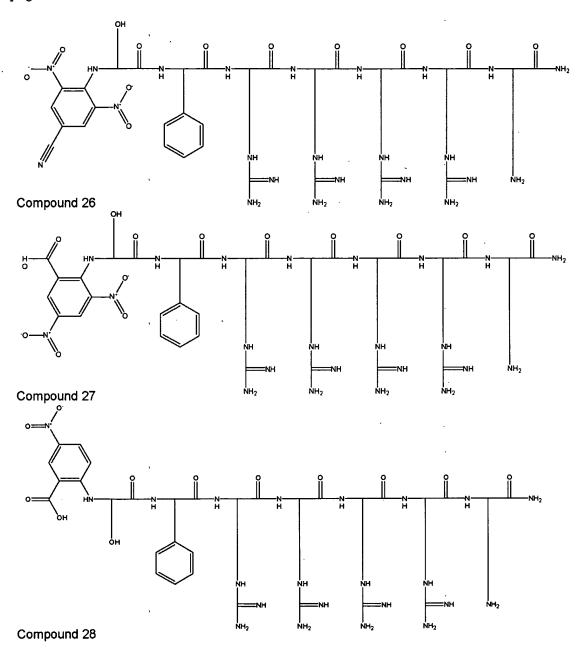
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#### Compound 20

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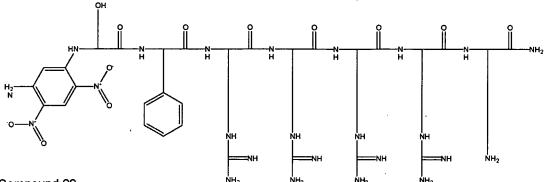
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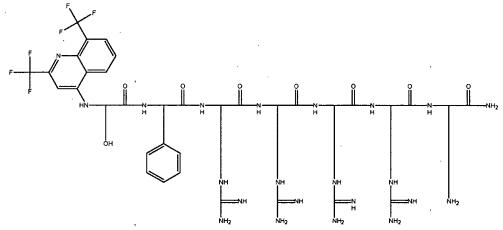


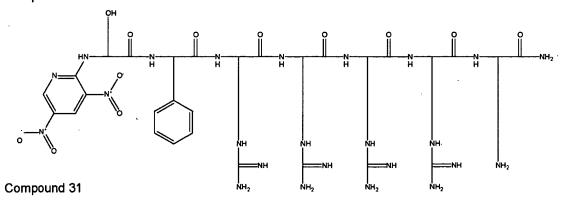
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# Compound 29





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# Compound 35

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# Compound 37

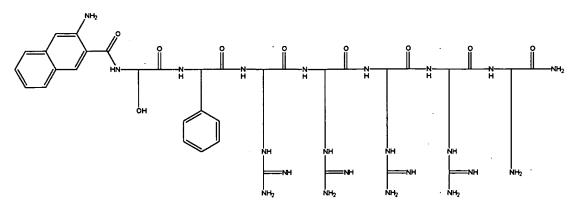
# Compound 38

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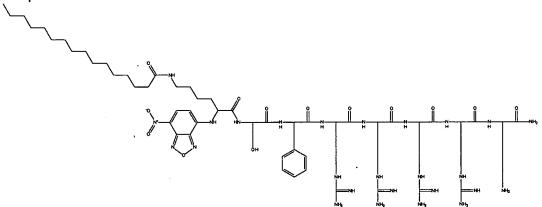
# Compound 40

# Compound 41

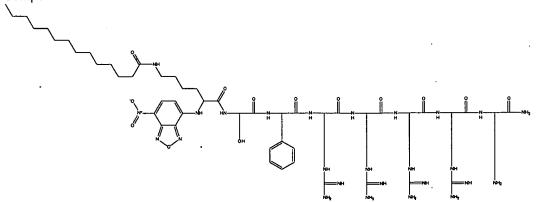
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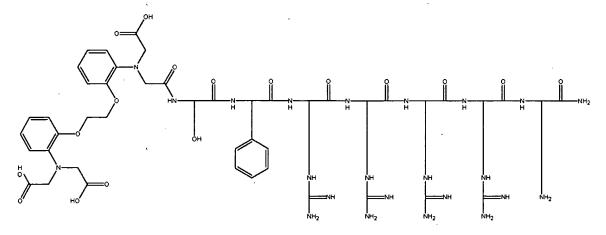
# Compound 43



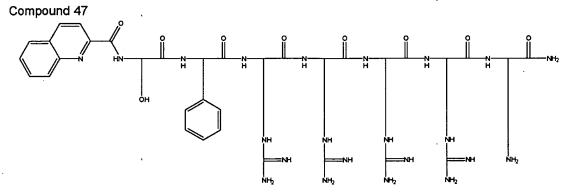
#### Compound 44



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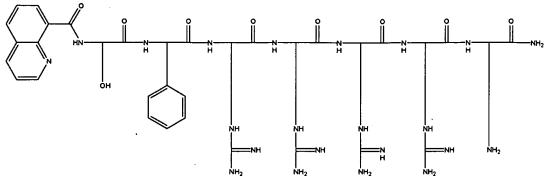


# Compound 46



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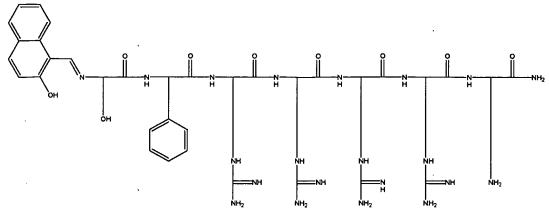
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# Compound 49

## Compound 50

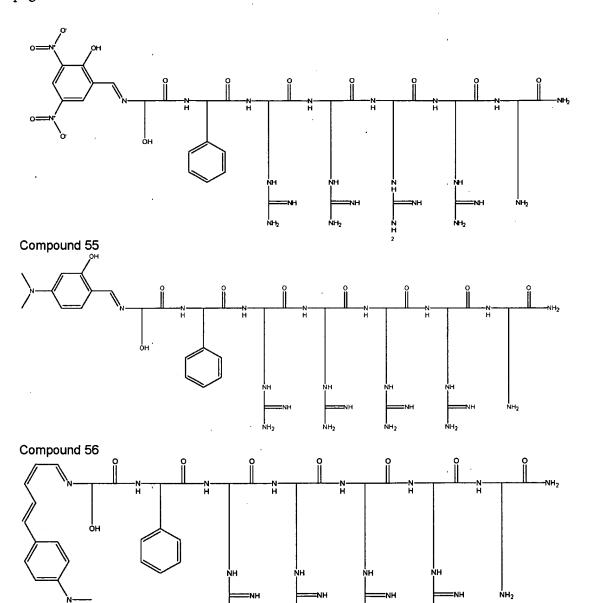
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# Compound 52

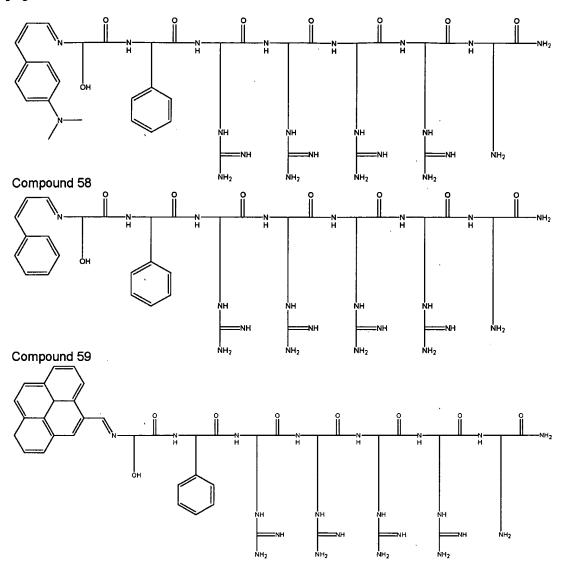
#### \*Compound 53

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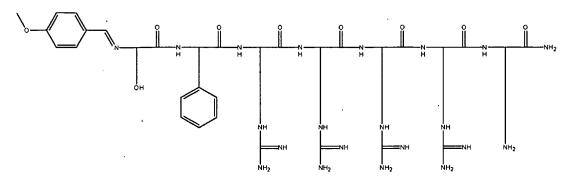


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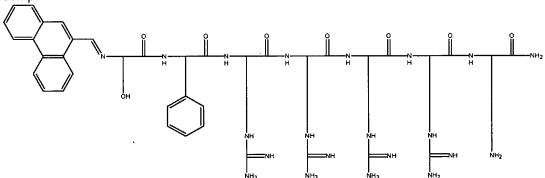


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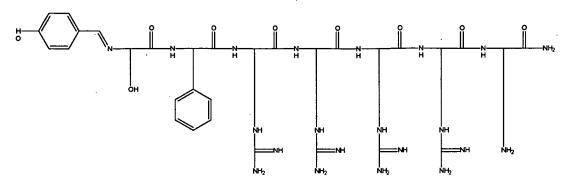


# Compound 61

# Compound 62

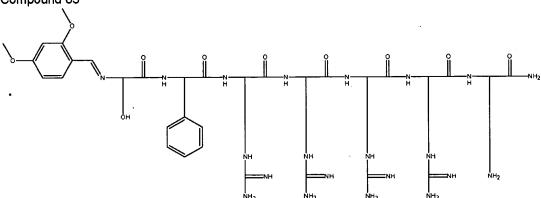


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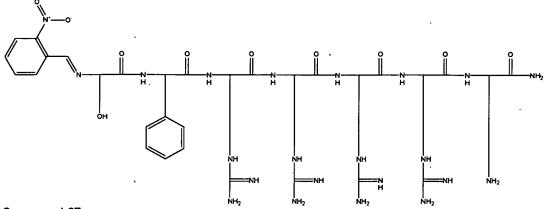
# Compound 64

# Compound 65



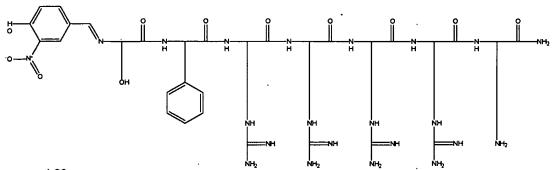
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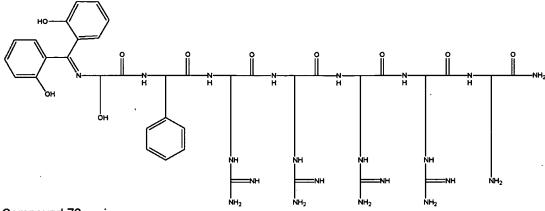


# Compound 67

## Compound 68



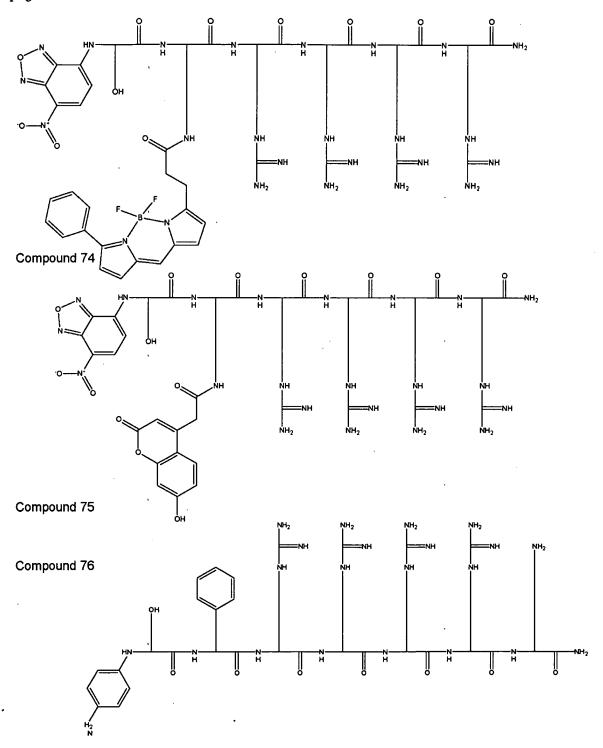
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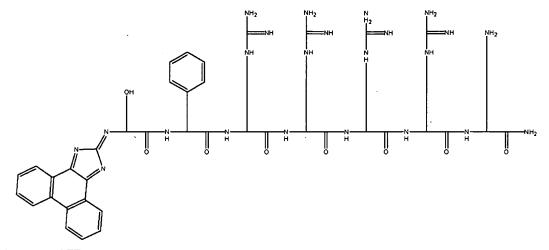
Compound 71

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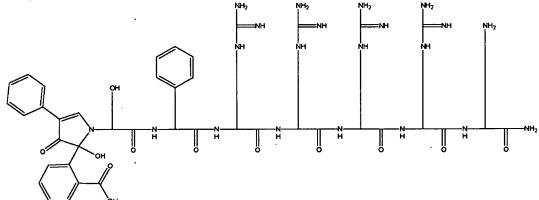
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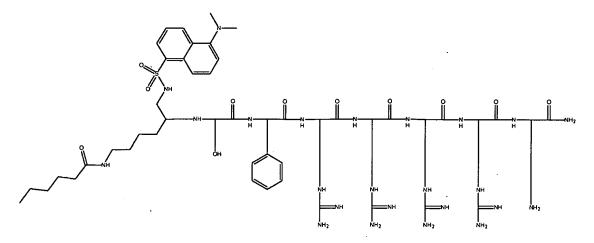
Compound 77



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Compound 80

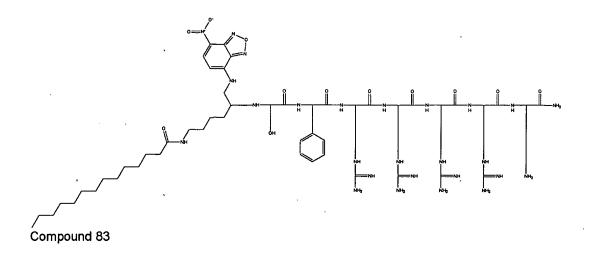
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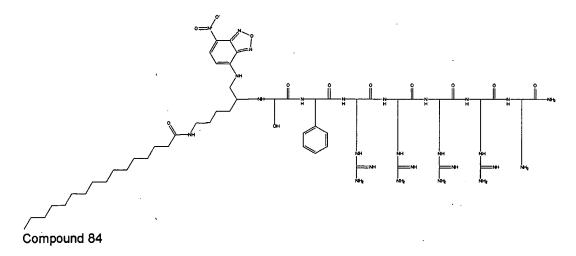


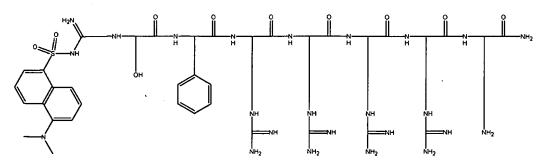
# Compound 81

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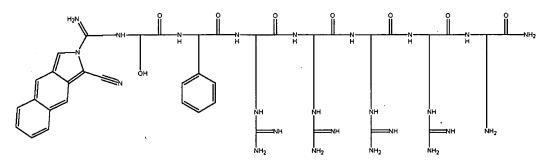
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### Compound 86

#### Compound 87

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### Compound 89

### Compound 90

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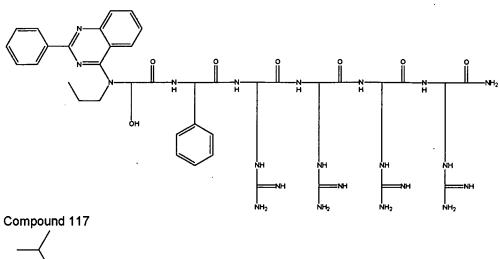
Compound 110

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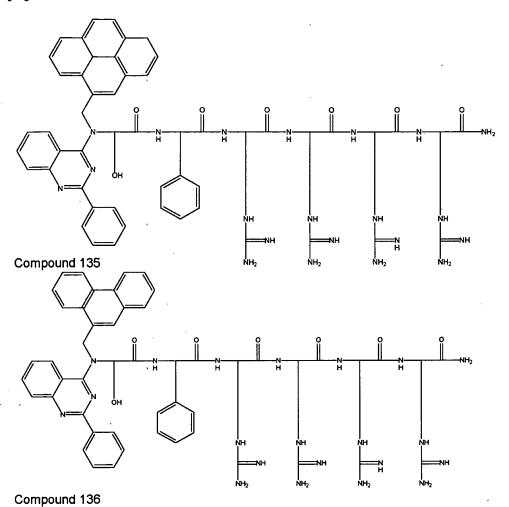
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# Compound 131

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Compound 138

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### Compound 143

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Compound 147

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## Compound 186

# Compound 187

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## Compound 201

Compound 202

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## Compound 203

## Compound 204

Compound 205

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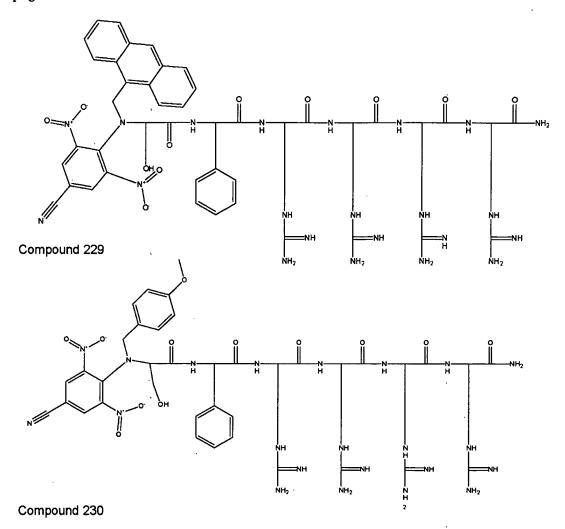
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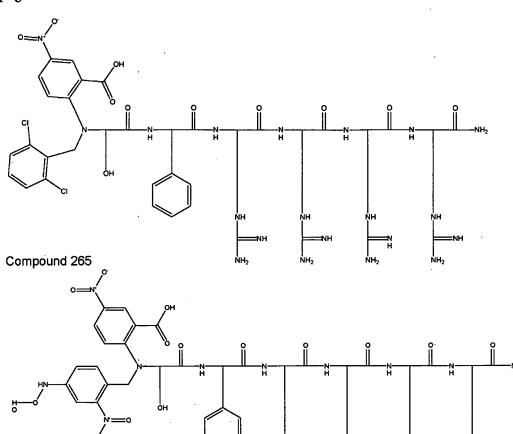
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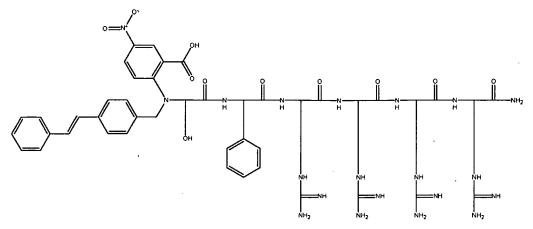


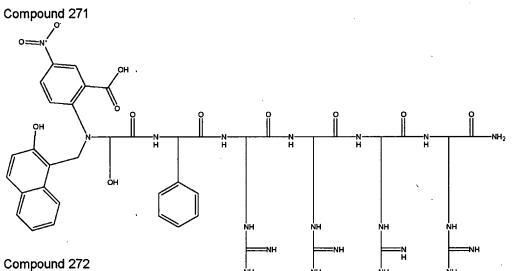
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Compound 303

Compound 304

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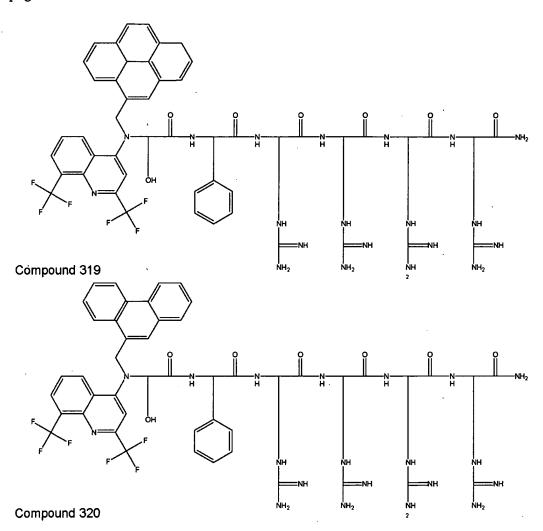
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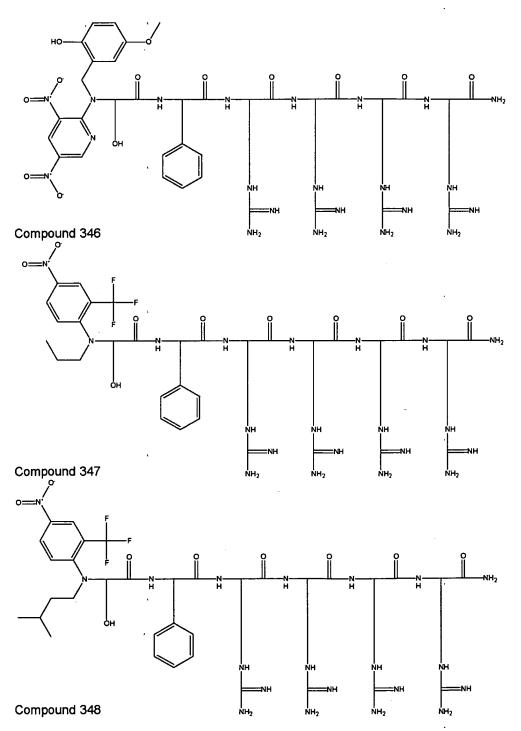
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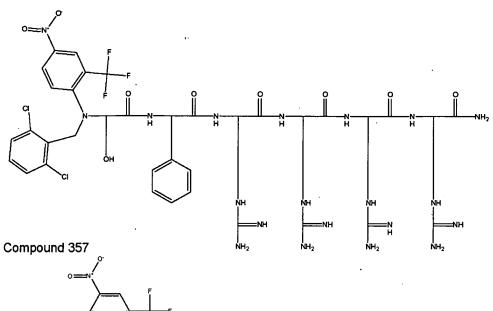
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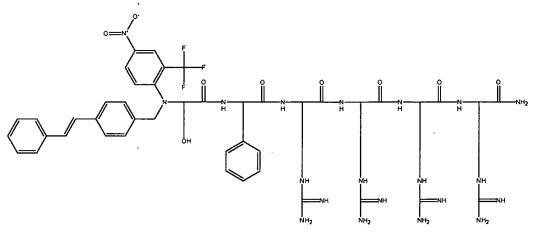


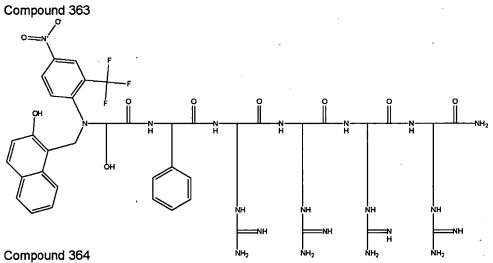
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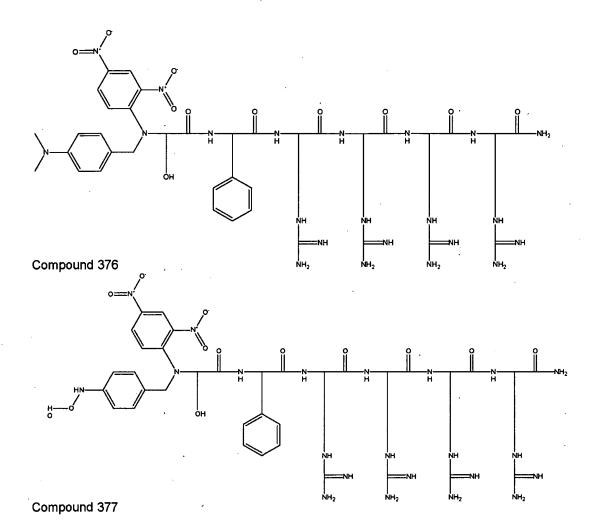
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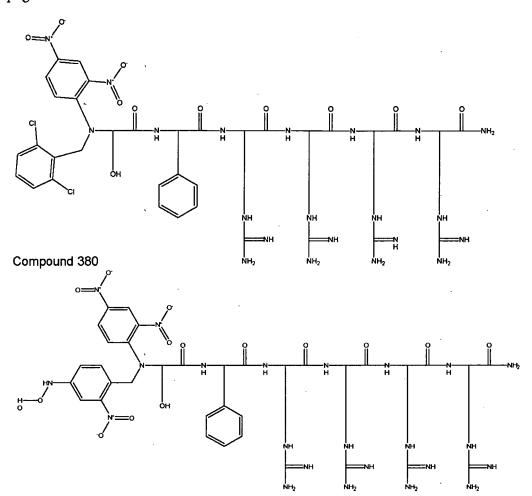
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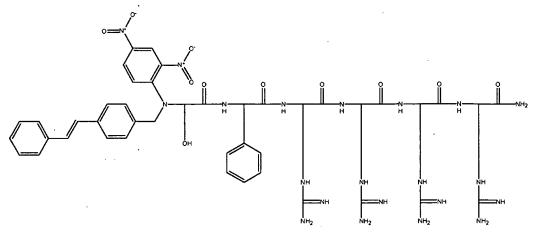


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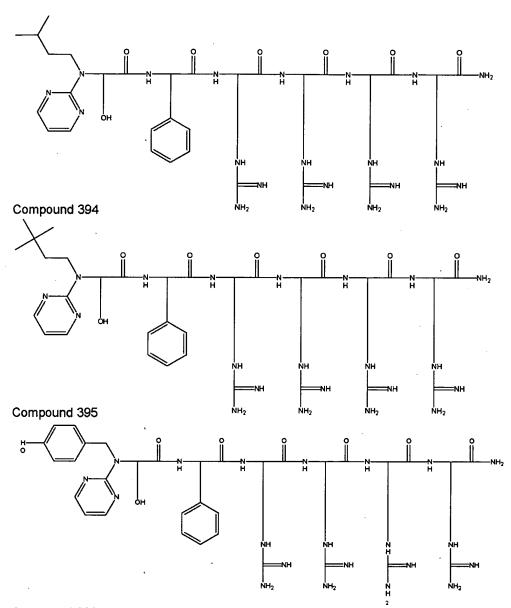
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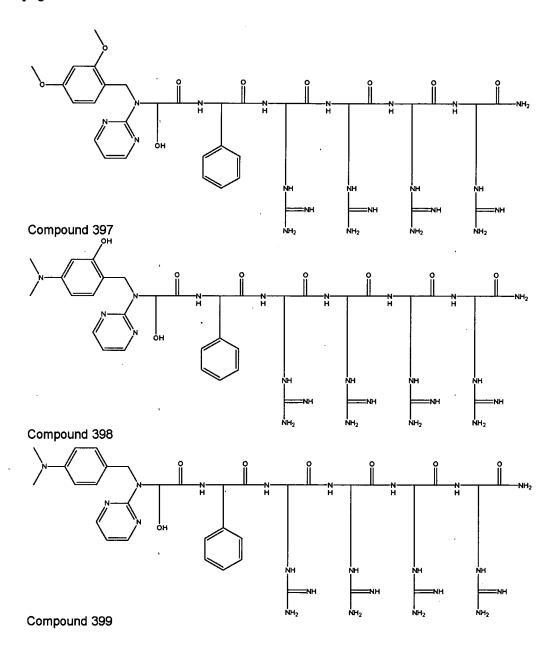
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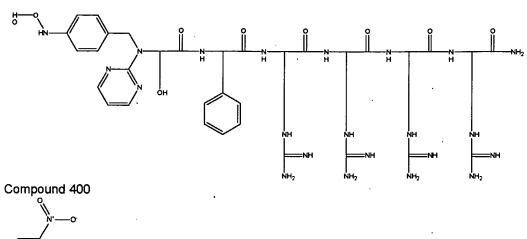
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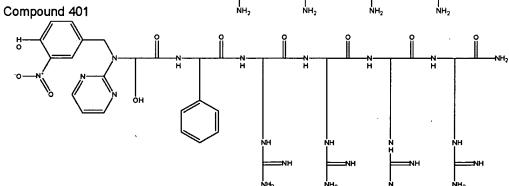


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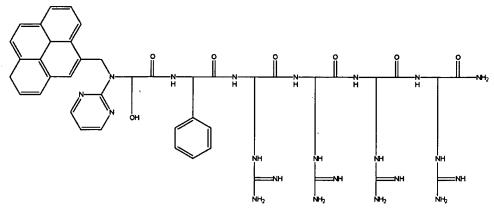
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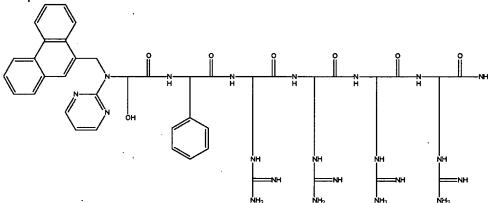
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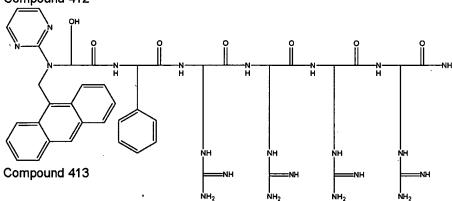
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### Compound 411



# Compound 412



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# wherein amino acid chains are indicated as follows:

- -OH represents serine,
- -NH<sub>2</sub> represents lysine,

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# 89. (Original) A chemical compound having the structure:

wherein the LINKER is selected from the group consisting of the following:

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90. (Currently amended) A chemical compound having the structure:

fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, and wherein the linker is selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

- 91. (Original) The chemical compound of claim 90, wherein the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative.
- 92. (Withdrawn and Currently amended) The chemical compound of claim 90, wherein the fluorophore <u>comprises</u> is a fluorescein <u>group</u> <u>derivative</u>.

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- 93. (Withdrawn and Currently amended) The chemical compound of claim 90, wherein the fluorophore comprises is selected from the group consisting of a dansyl group derivative, an acridine group derivative, an Alexa Fluor group derivative, a BODIPY group derivative, an Oregon Green group derivative, a Rhodamine Green group derivative, a Rhodamine Red-X group derivative, a Texas Red group derivative, a Cascade Blue group derivative, a Cascade Blue group derivative, a Pacific Blue group derivative, an AMCA-X group derivative, or and a coumarin group derivative.
- 94. (Withdrawn) The chemical compound of claim 90, wherein the linker is a metal chelating linker.
  - 95. (Canceled)
- 96. (Withdrawn and Currently amended) The chemical compound of claim 90, A chemical compound having the structure:

fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3); wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, wherein the linker is selected from the group consisting of N-methyl glycine, L-proline, D-proline,

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97. (Currently amended) The chemical compound of claim 90, A chemical compound having the structure:

fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, wherein the linker is selected from the group consisting of the following:

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- 98. (Original) The chemical compound of claim 90, wherein the chemical compound is a substrate for a protein kinase.
- 99. (Original) The chemical compound of claim 98, wherein the chemical compound is specific for protein kinase C.

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100. (Original) The chemical compound of claim 99, wherein the chemical compound is specific for isoforms  $\alpha$ ,  $\beta$ , and  $\gamma$  of protein kinase C.

101. (Withdrawn) The chemical compound of claim 98, the chemical compound is specific for protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca<sup>+</sup>/calmodulin-dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2 kinase.

102. (Original) The chemical compound of claim 90, wherein the chemical compound further comprises a carbohydrate, a lipid or a nucleic acid.

103-121. (Canceled)

122. (Currently amended) A chemical compound having the structure

$$\begin{array}{c} O_2N \\ OCH_3 \\ O_2N \\ O-N \end{array}$$
 Phe-Arg-Arg-Arg-Arg-Lys-amide 
$$(SEQ\ ID\ NO:3).$$

123. (Previously presented) A composition comprising a chemical compound of claim 89, and a carrier.

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124-126. (Canceled)

127. (Previously presented) The substrate of claim 60, wherein the substrate

comprises a metal ion chelator.

128. (Original) The substrate of claim 127, wherein the metal ion is a magnesium

ion or a calcium ion.

129. (Previously presented) The chemical compound of claim 90, wherein a metal

ion chelator induces a change in fluorescence intensity.

130. (Original) The chemical compound of claim 129, wherein the metal ion is a

magnesium ion or a calcium ion.

131. (Original) The chemical compound of claim 129, wherein the change in

fluorescence intensity is at least a 20% change in fluorescence intensity.

132. (Canceled)

133. (Previously presented) The chemical compound of claim 90, wherein the

linker comprises a turn to position the fluorophore in a location closer to the serine, the

threonine or the tyrosine than the location the fluorophore would occupy in the absence

of a turn in the linker.

134. (Previously presented) The chemical compound of claim 89, wherein the

linker comprises a turn to position the fluorophore in a location closer to the terminal

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serine, the terminal threonine or the terminal tyrosine than the location the fluorophore would occupy in the absence of a turn in the linker.

135-136. (Canceled)

137. (Previously presented) The composition of claim 123, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

138. (Previously presented) A composition comprising the substrate of claim 49, and a carrier.

139. (Previously presented) The composition of claim 138, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

140. (Previously presented) A composition comprising the compound of claim 88, and a carrier.

- 141. (Previously presented) The composition of claim 140, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 142. (Previously presented) A composition comprising the compound of claim 90, and a carrier.

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143. (Previously presented) The composition of claim 142, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

144-145. (Canceled)

- 146. (Previously presented) A composition comprising the compound of claim 122, and a carrier.
- 147. (Previously presented) The composition of claim 146, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 148. (Previously presented) The substrate of claim 56, wherein a photolabile side chain is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the substrate.
  - 149. (New) A composition comprising the substrate of claim 83, and a carrier.
- 150. (New) The composition of claim 149, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.